

Valorization of Coffee

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ABSTRACT

Coffee is one of the most consumed beverages in the world. Coffee is a complex mixture of thousands of chemicals. People's reactions to coffee or caffeine also vary from person to person. Low to moderate doses of caffeine (50-300mg) increase alertness, energy and ability to concentrate while higher doses can produce negative effects such as anxiety, irritability, insomnia and increased heart rate. The current review provides an overview of coffee and its constituents; as well as their relationship to various diseases and their role in the treatment of cancer, type 2 diabetes, heart health, depression, neurodegenerative diseases, gallstones and mortality.

KEYWORDS: coffee, caffeine, chemical constituents, uses, antioxidants

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INTRODUCTION

Coffee is a drink made from roasted coffee beans, which are made from the seeds of the *Coffea arabica* and *Coffea robusta* plant. It is dark, bitter, slightly acidic and has a stimulating effect on the human body mainly due to its caffeine content, which makes it one of the most widely consumed drinks in the world. There are many types of coffee plants with a complex taxonomy, the most common being Arabica coffee and Robusta coffee. In fact, coffee offers very few active supplements but it contains thousands of naturally active chemicals such as carbohydrates, lipids, nitrogen compounds, vitamins, minerals, alkaloids and phenolic compounds many of which can have beneficial effects on health.



Figure 1 Roasted and green beans of coffee

Origin and Distribution of Coffee:

Few types of coffee have been reported, some of which are Arabica, Robusta and *Coffea charriariana*, a decaffeinated coffee found in Cameroon. Coffee is a member of the Rubiaceae family which is also referred as breadfruit family. The coffee classification status is as follows-

Table 1 Taxonomic Position of Coffee

Kingdom	Vegetable
Subkingdom	Angiospermae
Class	Dicotyledoneae
Subclass	Sympetalae/Metachlamydeae
Order	Rubiales
Family	Rubiaceae
Genus	Coffea
Subgenus	Eucoffea
Species	C.arabica, C.robusta

Coffee production in India is dominated by the mountainous regions of the southern Indian states, with Karnataka accounting for 71% (Kodagu alone produces 33% of India's coffee), followed by Kerala at 21%, and Tamilnadu (5% of total production, 8,200 tons). Indian coffee is said to be the best shade coffee in the world, not direct sun coffee. Coffee is grown in three regions of India, with the states of Karnataka, Kerala and Tamil Nadu constituting the traditional coffee growing regions, followed by Andhra Pradesh and Odisha on the east coast of the country, the third

region includes Assam, Manipur, Meghalaya, Mizoram, Tripura, Nagaland and Arunachal Pradesh. The United States Food and Drug Administration (FDA) recognizes caffeine as a safe source both as a drug and as a food additive. In prescription and over-the-counter (OTC) medications, caffeine is used to treat fatigue and drowsiness, and to enhance the effects of certain pain relievers. It belongs to a group of medicines called central nervous system (CNS) stimulants. Foods that contain caffeine can help restore mental alertness.

Active Constituents of Coffee:

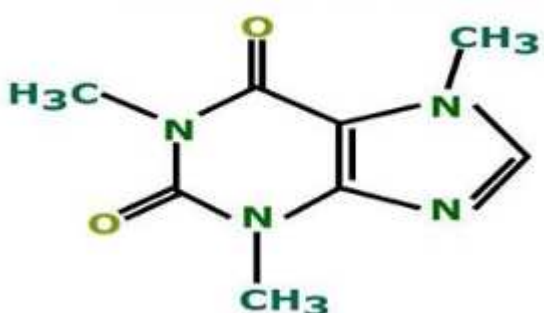
Coffee is rich in a variety of biologically active substances and coffee consumption has a variety of beneficial effects including central nervous system stimulants, Parkinson's disease, Alzheimer's disease, antidepressants, antioxidants, blood pressure maintenance, anti-inflammatory, asthma, Vascular dilators, cardiac stimulants, hypoglycemic agents, etc. improve liver detoxification. Although a large number of compounds have been isolated from various parts of coffee, some of them are:

Table 2 Biological Activities Of Some Coffee Constituents. [1,2,3,4,5]

Sr. No	Active Constituents	Parts Of Coffee plant	Biological Activity
1	Caffeine	Coffee beans	CNS Stimulant Antiparkinson Antialzheimer Antidepressant
2	Vitamins, minerals,	Coffee Leaves	Antioxidants
3	Chlorogenic Acid	Coffee Roots	Maintain Blood Pressure Antioxidant Weight Loss
4	Polyphenol	Coffee Pulp	Antioxidant Anti-inflammatory
5	Theophylline	Coffee Beans	Anti Asthmatic
6	Theobromine	Bean Husk/Bark	Vasodilator Aid In Urination Heart Stimulant
7	Diterpenes	Coffee Beans	Anticancer Improves liver detoxification
8	Trigonelline	Roasted Coffee Beans	Hypoglycemic Agent

1. Caffeine:

Structure of Caffeine



Caffeine (C₈H₁₀N₄O₂) is an alkaloid whose chemical name is 1,3,7-trimethylxanthine (1,3,7-

trimethyl-1H-purine-2,6(3H,7H)-dione) is one of the most commonly consumed stimulant alkaloids of methylxanthine category.^[6] It contains two fused purine-bound rings.^[7] Its physiological effects are mediated by rapid absorption from the gastrointestinal tract most commonly in caffeinated beverages. Caffeine has multiple molecular actions including the ability to act as an inhibitor of phosphodiesterase, ryanodine and adenosine receptors agonist. In addition to having various cytoprotective properties through its antioxidant effects and it also has ability to inhibit carcinogenesis.

2. vitamins and minerals:

Coffee contains many useful nutrients including riboflavin (vitamin B2), niacin (vitamin B3), magnesium, potassium, and various phenolic compounds or antioxidants. These and other components contained in coffee can benefit the body in various ways.

Table 3 The mineral and vitamins concentrations in 100 ml of coffee

Micronutrient	Per 100 ml (1 dl)	Per cup of coffee (1.25 dl)
Sodium	Very little	Very little
Potassium	92 mg	115 mg
Magnesium	8 mg	10 mg
Manganese	0.05 mg	0.06 mg
Riboflavin	0.01 mg	0.01 mg
Niacin	0.7 mg	0.9 mg

3. Chlorogenic Acid:

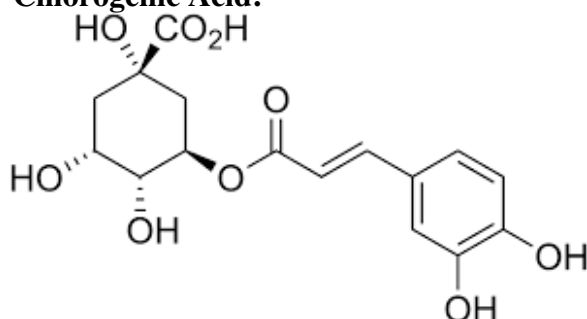


Figure 3 Structure of chlorogenic acid

A cup of coffee already contains enough chlorogenic acids to significantly lower a person's blood sugar levels and regular coffee drinkers are much less likely to develop type 2 diabetes or liver damage. Chlorogenic acids themselves have low bioavailability but they provide excellent substrates for gut bacteria and are converted into a range of bioavailable bacterial metabolites, which can have positive health effects.



Figure 4 Chlorogenic acid in green and roasted coffee

Robusta coffee has higher degree of diacyl chlorogenic acids. Additionally Robusta coffee contains chlorogenic acids and trihydroxycinnamic acids, such as sinapinic acid, which are not found in Arabica coffee beans.

4. Polyphenols:

Coffee beverages are a rich source of bioactive compounds especially polyphenols such as phenolic acids mainly chlorogenic (in green beans) and caffeine (produced after roasting). Other phenolic acids in coffee beans mainly include ferulic and p-coumaric acid. These compounds contribute to the overall intake of dietary polyphenols to benefit the consumer health.^[8] Polyphenolic compounds are well-known as natural plant insecticides. For human health polyphenols are powerful antioxidants that can prevent many non-communicable diseases.

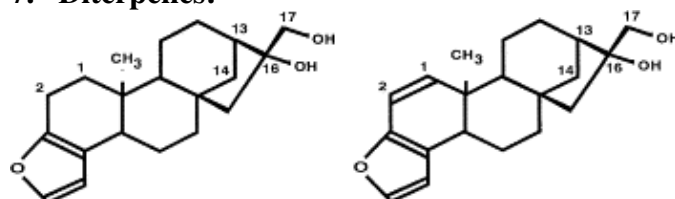
5. Theophylline:

unroasted coffee beans contains at around 5 mg/kg of theophylline. Theophylline is also known as 1, 3-dimethylxanthine, is a phosphodiesterase inhibitor used in the treatment of respiratory diseases such as chronic obstructive pulmonary disease (COPD) and asthma under various brand names. A member of the xanthine family, it has structural and pharmacological similarities to theobromine and caffeine, and is readily found in nature, in tea (*Camellia sinensis*) and cocoa (*Theobroma cacao*). A small amount of theophylline is one of the products of the metabolic processing of caffeine in the liver. Theophylline relaxes the smooth muscles of the airways, allowing easier breathing, while stimulating the speed and force of heart contractions.

6. Theobromine:

It is primary alkaloid in coffee seed. It is extracted from the pods and used to synthesize caffeine. It has been used in various medicines. Theobromine is found in cocoa and chocolate drinks as well as various forms of chocolate candies. Green coffee beans also contain small amounts of theobromine. Theobromine is produced in the body even without dietary intake, as it is a product of the body's metabolism of caffeine, which is metabolized in the liver to 12% theobromine, 4% theophylline and 84% paraxanthins. In the liver, theobromine is metabolized to xanthines and then to methyluric acid.^[9] Theobromine has an elimination half-life of 6-8 hours.^[10]

7. Diterpenes:



Cafestol

Kahweol

Figure 5 Structure of Cafestol and Kahweol

Kahweol and cafestol are diterpenoid molecules present in coffee as fatty acid esters and contribute to

coffee bitterness. These compounds are common in brewed and unfiltered coffee and can be removed by filtration. Kahweol and cafestol give coffee anti-cancer activity.

8. Trigonelline:

Trigonellin, pyridine-3-carboxylate N-methylbetaine, is present in coffee beans in amounts that depend on the coffee variety. Arabica Green Coffee contains 1% Trigonellin, 0.7% Robusta and 0.25% Liberia.

Coffee as medicine:

Coffee contains a variety of compounds that have recently been reported to have health benefits. Numerous studies have concluded that drinking coffee has health benefits, including reducing the risk of stroke in women, reducing the likelihood of

colorectal cancer by 26%,^[11] reducing the risk of type 2 diabetes and high blood pressure, the risk of cardiovascular diseases such as obesity and depression. It has also been reported as a stimulant, comfort food, condiment and confectionery and has effects on mental responses (alertness, mood changes), nervous system (childhood ADHD, Alzheimer's and Parkinson's diseases) and disorders metabolic (diabetes, gallstones, cirrhosis) have positive effects on gonadal and hepatic function.^[12] Coffee is actually a very healthy stimulant. It contains beneficial antioxidants and nutrients that can improve health. Its main function is to stimulate the central nervous system, cardiovascular muscles, respiratory system, diuresis and delay fatigue.



Figure 6 Coffee Pulp and Coffee fruit (Green beans)



Figure 7 Coffee Leaves and Coffee Bark



Figure 8 Roasted coffee beans and Coffee Roots

The above table summarizes some of the medicinal properties of the different parts of coffee:

Table 4 Medicinal attributes of various parts of coffee

Sr. No.	Parts	Medicinal Uses
1	Coffee Beans	CNS Stimulant, Antidepressant, Antiparkinson, Antiasthmatic, Antialzheimer, Anticancer, Improves Liver Detoxification, Hypoglycemic agent.
2	Coffee Roots	Maintain blood pressure, Antioxidant ,Anti-inflammatory
3	Coffee Bark	Vasodilator, Aid in urination, Heart stimulant
4	Coffee Pulp	Antioxidant ,Anti-inflammatory
5	Coffee Leaves	Antioxidant.

The objective of this review is to identify the different constituents of coffee and their roles in various disease states:

1. Chemotherapeutic effect of coffee:

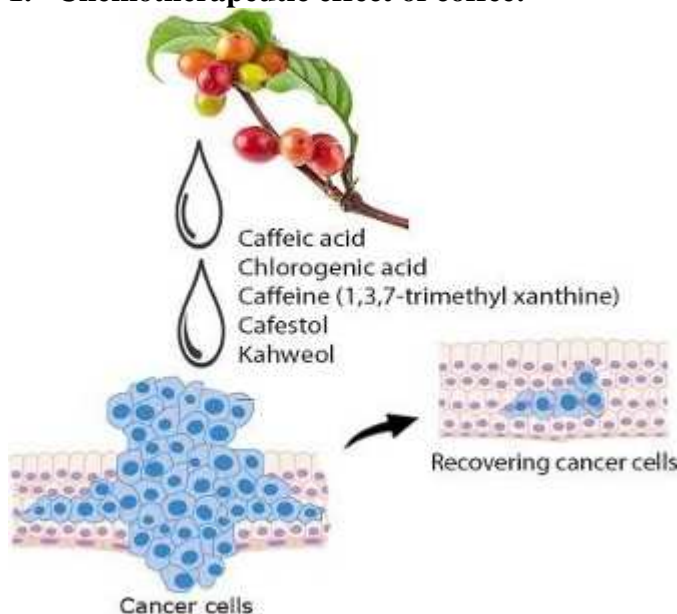


Figure 9 Coffee as anticancer

The International Agency for Research on Cancer (IARC) classified coffee as not carcinogenic to humans in 2016. Compounds derived from coffee have been shown to increase energy expenditure, regulate genes related to the repair of DNA and suppress chronic inflammatory responses. The chemopreventive effect of coffee depends on gene expression regulatory mechanisms involved in the processes of detoxification, metastasis, angiogenesis, apoptosis, inflammation and DNA repair.^[13] Coffee may protect against colorectal cancer by increasing colonic motility in the rectosigmoid region. The cafestol and kahweol content of coffee exhibits antioxidant properties by promoting the release of natural sterols and bile acids in the colon. The caffeine in coffee inhibits the growth of colon cancer cells. According to a 2015 report by the International World Cancer Research Fund, high coffee consumption is a potential protective measure against

liver cancer. Women who drank 6 or more cups of coffee a day had a statistically lower risk of breast cancer. The caffeine content of coffee may protect against the risk of breast cancer in women with mutations in the BRCA1/2 (breast cancer) gene.^[14] Coffee consumption is associated with a reduced risk of cancers of the oral cavity, pharynx, liver, colon, prostate, endometrium, and melanoma.

2. Coffee and fertility:

The effects of coffee on male and female fertility are shown in Table 5:

Table 5 The effect of coffee on fertility of men and women

Men	Women
High doses of caffeine might affect the quality of sperm.	High doses of coffee are likely to have some negative effects on fertility of women.

3. Effect Of Coffee On Memory:

Coffee has a positive effect on short-term memory by acting on the prefrontal cortex of the brain. Caffeine can improve long-term memory. Koppelstaetter et al used functional magnetic resonance imaging (fMRI) to determine how coffee activates different areas of the brain.^[15]

4. Lipid lowering effect of coffee:

3T3-L1 adipocytes (Vitro Model of White Adipocytes) were used to evaluate the effect of coffee cherries of different colors (green, yellow and red) on lipogenesis and/or lipolysis, and the results showed that the different colors of green coffee cherries all inhibited 3T3- Adipogenic activity of L1 adipocytes. A meta-analysis of 14 randomized controlled trials examining the effect of coffee consumption on serum cholesterol concentrations showed that brewed coffee consumption was dose-dependently associated with higher serum total and LDL cholesterol concentrations (low density lipoproteins).

5. coffee effect on diabetes:

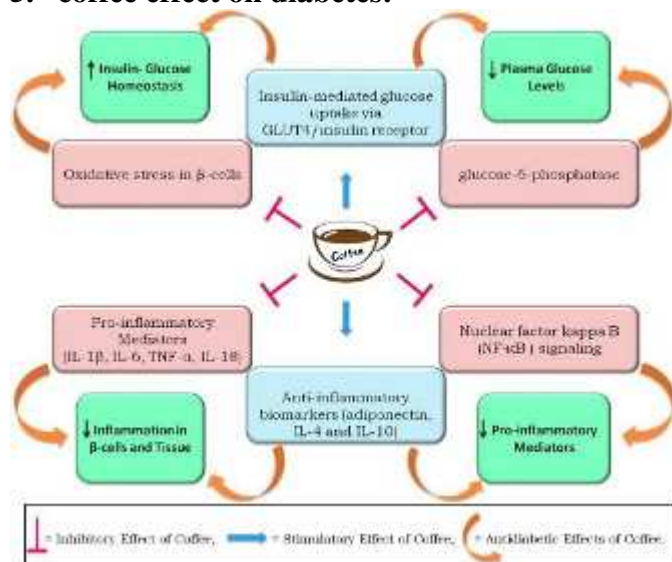


Figure 10 Coffee as anticancer

High coffee consumption is associated with a lower risk of type 2 diabetes and better glucose tolerance. Theophylline, a metabolite of caffeine in the liver, exerts antidiabetic effects by controlling glucose metabolism. Chlorogenic acid exhibits antidiabetic activity by reducing glucose production by the liver, exhibits its antioxidant properties, and reduces glucose absorption in the intestine by inhibiting glucose-6-phosphate translocase. Chlorogenic acid has also been shown to inhibit incretin hormones in the gut and protect pancreatic beta cells from oxidative stress through its antioxidant properties.

6. Coffee effect on Alzheimer's and Parkinson's Disease:

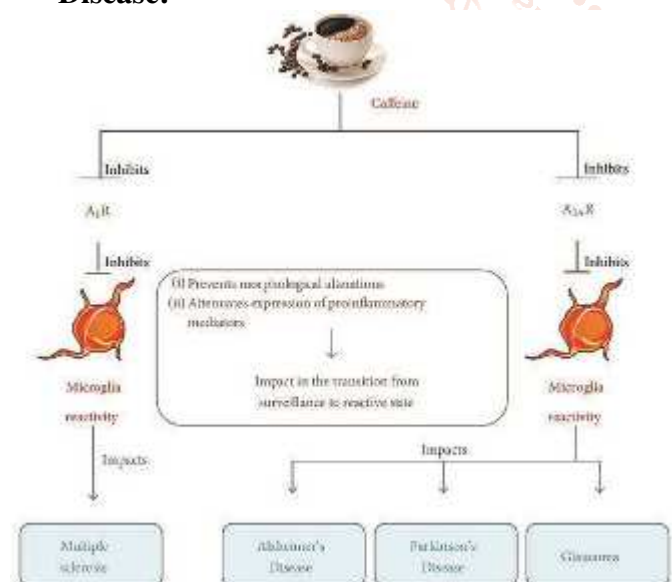


Figure 11 Coffee effect on Alzheimer's and Parkinson's Disease

Caffeine, an easily modifiable environmental factor which may have a protective effect on the likelihood of developing Alzheimer's disease. Caffeine, chlorogenic acid or their combination protects against central nervous system cognitive decline or biological

hallmarks of Alzheimer's disease. The caffeine in coffee is said to have a protective effect against Parkinson's disease. This mechanism is thought to be mediated by the action of caffeine on adenosine A2 receptors. According to reports, drinking 2-3 cups of coffee a day can prevent Parkinson's disease and Alzheimer's disease.^[16]

7. Coffee effect on anti-inflammatory, antioxidant and antibacterial activity:

The methanolic extract of green coffee beans has certain anti-inflammatory properties. The antimicrobial mechanism of hydrogen peroxide produced by mixing coffee with wound fluid and hypertonic sap killed bacterial cells. Coffee powder produced better wound healing than foam pads and saline gauze and it caused less cell detachment from the wound surface known as a topical dressing, it accelerates the growth of new cells with therapeutic properties. Ground coffee allows faster healing at all stages of wound healing, shortening inflammation, collagen proliferation and better epithelialization.^[17] Dressings containing ground coffee prevent bacterial contamination and play an active role in the healing process. It reduces the production of inflammatory cytokines (TNF- α , IL-1, IL-6, IL-12).

8. Effect of Coffee on Liver:

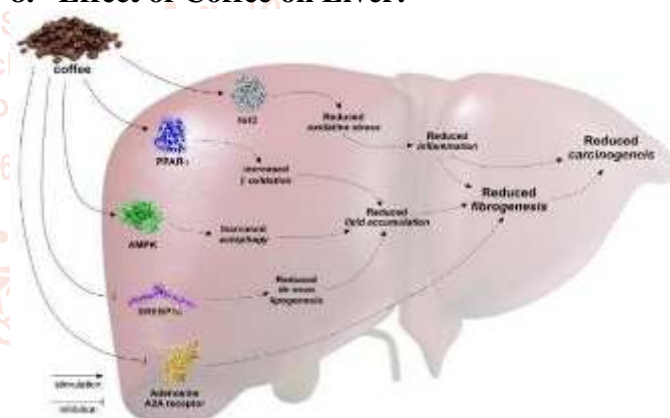


Figure 12 Coffee effect on liver

Liver fibrosis occurs in most types of chronic liver disease. Advanced fibrosis leads to cirrhosis, liver failure, and portal hypertension, often requiring liver transplantation. Caffeine is thought to play a role in preventing liver fibrosis. Caffeine is also thought to affect the liver detoxification process by activating uridine 50-diphosphate-glucuronosyltransferase. Coffee consumption was associated with higher concentrations of adiponectin, lower concentrations of markers of inflammation, and lower levels of markers of liver damage.

9. Coffee extract as weight loss supplement:

Green coffee extract is marketed as a weight loss supplement under various brand names such as "Coffee Slender" and "Svetol". An inverse association

between coffee consumption and weight gain has been reported in human subjects.^[18] Coffee consumption has also been shown to cause changes in several blood sugar markers in older adults. Green coffee extract is also thought to alter hormone secretion and glucose tolerance in humans.^[19]

10. Effect of coffee on attention:

A1 receptors are widely distributed throughout the brain and are particularly abundant in the hippocampus, cerebral cortex, and cerebellum as well as in many hypothalamic nuclei. They inhibit the release of various neurotransmitters such as glutamate, dopamine and acetylcholine. By binding to A1 receptors, caffeine blocks this inhibition, increasing neuronal activity. This results in an increase in wakefulness, alertness and concentration. In contrast, A2a receptors are concentrated in the striatum and have been shown to inhibit psychomotor function. Caffeine competes with adenosine at the A2 receptor and blocks this inhibition, which explains caffeine's ability to enhance psychomotor activity.

Coffee as cosmetic:

1. Skin Aging and Related Diseases:



Figure 13 Coffee effect on skin

The skin is the largest organ in the human body and has multiple functions among which protection against environmental factors is one of the most important. As we age, the skin becomes thinner, drier, wrinkled and becomes hyperpigmented. Skin aging is associated with matrix metalloproteinase-1-induced collagen fiber degradation and increased production of mitochondrial reactive oxygen species and oxidative stress, leading to common loss of mitochondrial DNA. Coffee is high in antioxidants especially chlorogenic acid and caffeine, two compounds that show promise for use in anti-wrinkle products. During the aging process, hyaluronic acid levels decrease and the skin becomes dry and wrinkled. Indeed, hyaluronidase degrades hyaluronic acid, reduces its viscosity, increases its permeability and leads to the destruction of the extracellular matrix (collagen and elastin fibers). In conclusion, coffee extract has the potential to be used as an ingredient in

skin cosmetics to reduce the generation of intracellular reactive oxygen species in keratinocytes and improve skin health.

2. Coffee as anti-inflammatory agents:

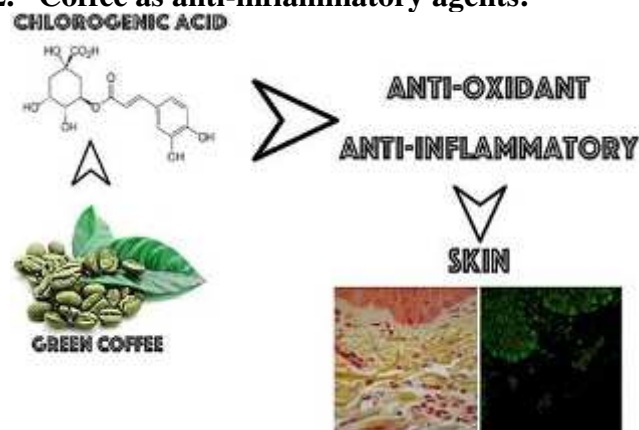


Figure 14 Coffee effect as anti-inflammatory

Skin inflammation can be defined as the skin's response to injury, infection, or destruction and is often characterized by warmth, redness, pain, swelling, or disruption of skin physiology. Anti-inflammatory effects of chlorogenic acid, a phenolic compound commonly found in coffee compositions. Interleukin-8 production in human intestinal cell lines is induced by combined stimulation of tissue necrosis factor- α and hydrogen peroxide. Chlorogenic acid and caffeic acid inhibit induced interleukin-8 production, suggesting a significant anti-inflammatory effect.^[20]

3. Anti acne effect of coffee:

Acne occurs when oil, dead skin cells, and other substances clog pores, which can become infected with bacteria and cause inflammation. Scrubbing the face with coffee grounds will help remove dead skin cells and unclog pores. The chlorogenic acids in coffee may also reduce inflammation and protect against certain bacteria.

4. Photoprotective property:

Palmitic acid-rich coffee bean oil has also shown strong potential as a natural sunscreen, showing high SPF, when used as the sole active ingredient in cosmetic formulations. The chlorogenic and caffeic acids in coffee extract reduce UV-induced photoaging by inhibiting the action of matrix metalloproteinases, a group of enzymes expressed during UV-B radiation that promote the breakdown of elastin fibers, and reduce by scavenging active oxygen.

5. Coffee as Hair Colourant:

Using pure instant coffee solution is an alternative coloring agent for dark brown hair and can cover gray hair, it also reduces scalp irritation, possibly due to the anti-inflammatory activity of the compounds phenolics. Coffee has a natural hair dye.

6. Coffee in soaps and scrubs:



Figure 15 Coffee Scrub

The coarse particles of coffee grounds act as an exfoliant, helping to remove dirt and dead skin cells. One of the main benefits of using a coffee scrub is its ability to exfoliate dead skin cells, reduce cellulite, firm skin and reveal brighter skin. The chlorogenic acids and hydrocarbons in coffee oil are able to self-assemble, forming stable micelles and reducing surface tension.

7. Antimicrobial activity of coffee:

Depending on the concentration, coffee melanoids can be bacteriostatic or bactericidal. Additionally, other coffee compounds naturally present in coffee extracts, including chlorogenic acid and caffeine, may interact synergistically to confer antimicrobial activity against *Streptococcus mutans*, a microorganism associated with plaque formation. In short, coffee extracts may have promising applications in infectious skin diseases and even as preservatives in final cosmetic formulations.^[21]

8. Anti-Hair loss Activity:



Figure 16 Coffee hair oil

Caffeine is increasingly used in the production of cosmetics to improve not only the appearance of the skin but also the condition of the hair due to its 5 α -

reductase inhibitory activity. This enzyme converts testosterone into the more active dihydrotestosterone (DHT), which can lead to hair loss due to the sensitivity of hair follicles to the effects of DHT. Caffeine renews the hair growth phase by inhibiting the activity of 5 α -reductase. Caffeine also stimulates microcirculation in the capillaries of the scalp, helping to care for the hair follicles. Caffeine's ability to penetrate hair follicles and stimulate human hair growth in vitro may have important clinical implications for the management of androgenetic alopecia, a common problem in men of all ages.^[22]

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